REMARKS

The Present Invention

The claimed invention is directed to methods for modifying the genotype or phenotype of a plant, preferentially in plant seed tissue, by transforming a plant with a DNA construct comprised of *i*) a transcriptional initiation or promoter region from a gene that is preferentially or specifically expressed or regulated in plant seed tissue; and *ii*) a DNA sequence of interest other than the coding sequence native to that gene.

The Pending Claims

Prior to entry of the above amendments, Claims 17-48 are pending. Claim 17 is directed to a method for obtaining a plant having a modified phenotype. Claims 18 and 27 are directed to a method for altering the phenotype of plant seed tissue as distinct from other plant tissue. Claims 19-26 and 42-45 depend from either Claim 17 or 18. Claims 28-33 are directed to a method for modifying the genotype of a plant to impart a desired characteristic to seed as distinct from other plant tissue. Claims 34-38, 46 and 47 are directed to a method for modifying transcription in seed tissue as distinct from other plant tissue. Claims 39-41 are directed to a method to selectively express a heterologous DNA sequence of interest in seed tissue as distinct from other plant tissue. Claim 48 is directed to a method to selectively express a heterologous DNA sequence of interest in plant seed tissue as distinct from other plant tissue.

The Office Action

The oath or declaration is defective.

The effective filing date for the instantly claimed application, drawn to seed-specific promoters and their use, is 31 July 1986, the filing date of parent application Serial No. 06/891,529 which was the earliest parent to teach such a promoter.

The specification is objected to for its inclusion of blanks on page 31, line 7.

Claims 17-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-11 of U.S. Patent No. 5,420,034.

Claims 17-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-14 of U.S. Patent 5,608,152.

Claims 17-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-14 of U.S. Patent 5,981,839.

Claims 18-33 and 42-47 are rejected under 35 U.S.C. 112, second paragraph.

Claims 28-33 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, on the basis that the specification does not enable claims broadly drawn to the use of any promoter or any regulatory sequence to effect seed-specific gene expression, transcription or phenotypic alteration.

Claim 42 is rejected under 35 U.S.C. 112, first paragraph, on the basis that the specification does not enable claims broadly drawn to any promoter from a cruciferin gene.

Claims 17-48 are rejected under 35 U.S.C. 112, first paragraph, on the basis that the specification does not meet the written description requirement.

Claims 28-29, 31 and 46-47 are rejected under 35 U.S.C. § 102(b) as being anticipated by each of Horsch et al. and DeBlock et al.

Claims 17-32, 34-37, 39-40, and 43-48 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zambryski et al. taken with Sengupta-Gopalan et al.

Claims 20, 33, 38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zambryski et al. taken with Sengupta-Gopalan et al. as applied to claims 17-32, 34-37, 39-40 and 43-48 above, and further in view of Pedersen et al.

Claims 17-32, 34-37, 39-40 and 43-48 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hall et al. (U.S. Patent 5,504,200) taken with Sengupta-Gopalan et al.

Claims 20, 33, 38 and 41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hall et al. (U.S. Patent 5,504,200) taken with Sengupta-Gopalan et al. as applied to claims 17-32, 34-37, 39-40 and 43-48 above, and further in view of Zambryski et al. taken with Pedersen et al.

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Claim 42 is deemed free of the prior art for the reasons presented in allowed parent and commonly-owned applications corresponding to U.S. Patents 5,420,034, 5,608,152 and 5,981,839.

Amendments

In the Specification

Amendments to page 1 of the specification were made to reflect that application serial no. 08/812,665 has issued as USPN 5,981,839; application serial no. 08/484,941 has issued as USPN 5,750,385 and application serial no. 08/105,852 has issued as USPN 5,753,475, and to correctly recite application serial no. 07/267,685. The filing receipt to application serial no. 07/267,685 is attached.

Minor amendments were made to certain of pages 18-75 of the specification to correct typographical errors.

In the Claims

Applicants have amended Claims 17, 18, 20, 23, 24, 26, 28, 33, 38, 41, 42 and 46-48, and added new Claims 49-62.

Support for amending Claim 17 is found on page 9, lines 1-11, page 15, lines 14-18 and on page 51, lines 12-15.

Support for amending Claim 18 is found in the preamble of the originally filed claim, and on page 9, lines 1-11, page 15, lines 14-18 and on page 51, lines 12-15.

Support for amending Claim 20 to recite a tomato plant is found on page 22, line 24.

Claim 23 was amended to an independent claim incorporating the language of Claim 17.

Claim 24 was amended to depend from both claims 23 and 52.

Claim 26 was amended to correct a typographical error.

Support for amending Claim 28 to recite "preferentially regulated in plant seed tissue" is found in originally submitted Claims 17 and 18. Support for amending the last line is found in the preamble of the originally filed claim.

Support for amending Claim 33 to recite a tomato plant is found on page 22, line 24.

Support for amending Claim 38 to recite a tomato plant is found on page 22, line 24.

Support for amending Claim 41 to recite a tomato plant is found on page 22, line 24.

Claim 42 was amended to an independent claim incorporating the language of Claim 17. In accordance with the Examiner's suggestion, this claim was also amended to recite appropriate Markush language.

Support for amending Claim 46 to recite "transcriptional initiation region" and "preferentially" expressed in plant seed tissue is found in originally submitted Claim 18. Support for amending the last line is found in the preamble of the originally filed claim.

Claim 47 was amended to properly depend from amended Claim 46.

Support for amending Claim 48 is found in originally submitted Claim 17.

Support for new Claim 49 is found in originally submitted Claim 42.

Support for new Claims 50 and 51 is found on page 14, lines 23-24 and on page 15, lines 14-16.

New Claim 52 is originally submitted Claim 23 made independent and incorporating the language of Claim 18. Support is also found on page 9, lines 1-11, page 15, lines 14-18 and on page 51, lines 12-15.

New Claim 53 is originally submitted Claim 42 made independent and incorporating the language of Claim 18. Support is also found on page 9, lines 1-11, page 15, lines 14-18 and on page 51, lines 12-15.

Support for new Claim 54 is found on page 20, line 20.

Support for new Claim 55 is found on page 22, lines 18-24.

Support for new Claim 56 is found in originally filed Claim 27.

Support for new Claim 57 is found in originally filed Claim 19.

Support for new Claim 58 is found in originally filed Claim 27.

Support for new Claim 59 is found on page 12, lines 9-11.

Support for new Claim 60 is found on page 12, lines 9-16.

Support for new Claims 61 and 62 is found on page 6, lines 15-16.

Applicants believe that no new matter has been added by any of these amendments and therefore respectfully request the Examiner to enter them.

Response

The Examiner's specific objections and rejections are reiterated below as small indented bold print, followed by Applicant's response in normal print.

Objections

The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. 1.67(a) identifying this application by application number and filing date is required. The inventors' signatures are not dated. Furthermore, parent application Serial No. 07/267,685 is incorrectly listed as 07/267,865.

Applicants submit herewith an executed, corrected declaration.

The specification is objected to for its inclusion of blanks on page 31, line 7.

Applicants have replaced blanks with the appropriate volume and page numbers for the cited reference.

Rejections

Obviousness-Type Double Patenting

Claims 17-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 5,420,034. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to utilize the DNA constructs containing a seed-specific promoter and plant cells containing them as claimed in the patent to obtain the DNA constructs containing a seed-specific promoter and methods for their use to obtain transformed plant cells and plants containing them as claimed in the instant application.

This rejection is avoided by the attached terminal disclaimer.

Claims 17-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent 5,608,152. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to utilize the plants and seeds containing DNA constructs containing a seed-specific promoter for seed-specific expression of heterologous genes as claimed in the

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patent to obtain the DNA constructs containing a seed-specific promoter and methods for their use to obtain transformed plant cells and plants containing them as claimed in the instant application.

This rejection is avoided by the attached terminal disclaimer.

Claims 17-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent 5,981,839. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to utilize the plants and seeds containing DNA constructs containing a seed-specific promoter for seed-specific expression of heterologous genes and transformed plant cells and plants containing them as claimed in the patent to obtain the DNA constructs containing a seed-specific promoter and methods for their use to obtain transformed plant cells and plants containing them as claimed in the instant application.

This rejection is avoided by the attached terminal disclaimer.

35 U.S.C. § 112, second paragraph.

Claims 18-33 and 42-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is indefinite for failing to positively recite an essential claim element, the alteration of phenotype of plant seed tissue as recited in the preamble, in the body of the claim. The last phrase of the claim is instead drawn to alteration of plant phenotype. Dependent claims 19-27 and 43-45 are included in the rejection.

Claim 28 is indefinite for failing to positively recite an essential claim element, the imparting of a distinct characteristic to seed as recited in the preamble, in the body of the claim. The last phrase of the claim is instead drawn to the modification of seed genotype; however, the genotype of every cell in the plant would be modified. Dependent claims 29-33 are included in the rejection.

Claim 42 is indefinite for failing to employ proper Markush terminology per MPEP 2173.05(h). Replacement of "or" in line 2 with -and—would obviate this rejection.

Claim 46 is indefinite for failing to positively recite an essential claim element, the modification of transcription in plant seed tissue as recited in the preamble, in the body of the claim. The last phrase of the claim is instead drawn to the expression of a DNA sequence of interest. Furthermore, the phrase "said regulatory regions" recited in lines 5 and 6 lacks antecedent basis in the claim in line 4. Replacement of "region" in line 4 with -regions—would obviate this portion of the rejection. Dependent claim 47 is included in the rejection.

Applicants have amended Claims 28-33 and 46-48 in accordance with the suggestions made by the Examiner. In Claims 18, 28 and 46, the essential claim elements recited in the preamble are now recited in the body of the claims. In addition,

Claim 46 has been amended to recite "transcriptional initiation region" instead of "regulatory region". Claim 42 now recites appropriate Markush language.

35 U.S.C. § 112, first paragraph.

> **Claims 28-33 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to the use of seed-specific promoters for seed-specific gene expression, transcription, or phenotypic alteration, does not reasonably provide enablement for claims broadly drawn to the use of any promoter or any regulatory sequence to effect seed-specific gene expression, transcription or phenotypic alteration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.**
>
> **The specification only demonstrates the use of three seed-specific promoters from the same plant family for the seed-specific expression of heterologous genes. No guidance is presented regarding the identification, isolation, or evaluation of constitutive or other types of tissue-specific promoters for their ability to effect seed-specific heterologous gene expression. Furthermore, no guidance is presented regarding the identification, isolation or evaluation of regulatory sequences other than promoters (as claimed in claims 46-47) for the seed-specific expression of heterologous genes. In contrast, the claims are broadly drawn to any type of promoter or regulatory sequence which would be sufficient to effect seed-specific gene expression.**
>
> **Furthermore, tissue-specific gene expression could be the result of a variety of complex factors other than a tissue-specific promoter immediately upstream of the structural gene. Such alternate factors include distant genes encoding regulatory proteins, activator/operator/repressor systems, far upstream or downstream enhancer elements, changes in the phosphorylation of transcriptional proteins, export of mRNA from DNA found in other organelles or tissues, transposable elements, and post-transcriptional controls such as alternative RNA splicing (see, e.g., Molecular Biology of the Cell, pages 553-569; 588-597, and 606-607).**
>
> **Thus, multiple attempts to isolate the putatively tissue-specific promoters associated with a multitude of genes encoding tissue-specific gene products could prove unsuccessful.**
>
> **Given the breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify, isolate and evaluate a multitude of non-exemplified promoter types or other types of regulatory sequences for their ability to effect seed-specific gene expression.**
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> **See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must apply the enabling aspects of the invention.**

Applicants respectfully traverse this rejection for the reasons set forth in the prior response. However solely in the interest of further prosecution, and not acquiescing to the rejection by the Examiner, Applicants have amended the claims. Further, Applicants maintain that the claims as originally filed are properly enabled by the specification for the reasons already made of record.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP 2164.01. Because the detailed guidance provided in Examples 2-6 on pages 35-63 teach methods applicable to any seed specific promoter, Applicants respectfully submit that the specification enables the skilled artisan to make DNA constructs for use in the claimed methods with any seed specific promoter. Claims 28 and 46 have been amended to recite that the transcriptional initiation region is from a gene that is preferentially regulated in a plant seed tissue. Claim 48 has been amended to recite a promoter region from a gene which is preferentially expressed in plant seed tissue. In view of these amendments, the Examiner is respectfully requested to withdraw this rejection.

> **Claim 42 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a claim limited to the three exemplified seed-specific promoters, does not reasonably provide enablement for claims broadly drawn to any promoter from a cruciferin gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.**
>
> **The specification only teaches the isolation of seed-specific promoters from three seed-specific genes from the same plant family. No guidance is provided regarding the identification or isolation of the cruciferin gene or its corresponding promoter, or for the evaluation of any putative cruciferin promoter for its ability to drive seed-specific gene expression.**
>
> **The tissue-specific regulation of gene expression, and existence of directly upstream tissue-specific promoters, is unpredictable, as taught by Molecular Biology of the Cell cited above.**
>
> **Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify and isolate a cruciferin gene, and to identify, isolate and evaluate any putative promoter for its ability to drive seed-specific expression of heterologous genes. See *Genentech* cited above.**
>
> **See also In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 USPQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein.**

In the interest of furthering prosecution, Applicants have removed "a cruciferin gene" from the Markush group of Claim 42, and added new Claim 49 to depend from Claim 17 or 18 and recite "wherein said gene is a cruciferin gene". Although it is redundant to do so, Applicants have further specified in both Claim 42 and Claim 49 that the transcription initiation region is from a gene that is preferentially expressed in

seed tissue. The Examiner's attention is particularly drawn to page 62, lines 29-31, where Applicants teach that cruciferin is a seed storage protein.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP 2164.01. Factors to be considered when determining whether any necessary experimentation is undue are recited in *In re Wands* and in MPEP 2164.01(a). On page 62, line 30 through page 63, line 2 of the specification, Applicants point out that *cDNA clones* (not just the protein) for cruciferin have been identified by Simon, *et al.* Furthermore, Laroch-Raynal and Delseny (*Eur. J. Biochem.* (1986) 157:321) demonstrate specifically using rapeseed cruciferin cDNA as a probe to identify precursors for radish storage proteins. The level of the skilled artisan in the field of the instant invention is high and sophisticated. The ordinarily skilled artisan could readily combine the detailed teachings provided in working Examples 2-6 on pages 35-63 of the instant application for identifying and isolating transcriptional initiation regions for napin, EA9 and acyl-carrier protein genes with the information available about cruciferin in the literature, to identify and isolate a transcriptional initiation region for a cruciferin gene that is preferentially regulated in plant seed tissue. Applicants have shown in four instances successful application of their method predictably carried out using the same molecular biology techniques. It would have been well within the abilities of the skilled artisan to logically carry out the individual steps required to identify the promoter region for the cruciferin gene, using the cDNA sequence that was in the public domain, and analogously applying the methods fastidiously demonstrated in Examples 2-6 of the instant application for the identification of the napin, EA9 and ACP promoter regions. The technical work involves identifying the 5' flanking sequence that includes the promoter region, but does not require undue experimentation nor is it entirely unpredictable, as demonstrated by the four successful examples provided herein, where the promoters are characterized sufficiently for isolation and subcloning independent from their native open reading

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frames. Applicants successfully achieved the claimed methods by isolating 5' flanking sequences of a predictable and consistent size range of 1.5 to 2.1 kb (*see* page 36, lines 19-21 for *B. napus* napin, page 53, line 20 for *B. campestris* napin, and page 58, lines 1-20 for *B. campestris* ACP). Additionally, Sengupta-Gopalen, *et al.*, in a reference cited by the Examiner, report successful expression of the bean β-phaseolin gene in the embryo tissue of tobacco plants by subcloning 863 bp of the 5' flanking region along with the native open reading frame, thereby providing a fifth example of a seed-specific promoter region that resides directly upstream of the open reading frame. It is submitted that the skilled artisan could use the cruciferin cDNA sequence with the methods and techniques outlined in Examples 2-6, to identify the promoter region with a reasonable expectation of success and without undue experimentation.

As a demonstration of the operability of the invention, Sjodahl, *et al.* (*Planta* (1995) *197*:264) evaluate expressing the cruciferin structural gene under the control of different truncated lengths of the cruciferin gene promoter. Their work demonstrates that promoter lengths of 974 bp or more comprise a functional cruciferin promoter that regulates seed-specific expression, a length well within the 5' flanking region that would have been isolated applying the methods set forth in the specification. Based on the information readily available to the skilled artisan at the time of application and the detailed teachings provided by the instant specification, Applicants respectfully assert that the skilled artisan would have been able to successfully make and use a promoter from a cruciferin gene preferentially expressed in seed in the claimed methods without undue experimentation. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Claims 17-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any type of promoter or regulatory region of any length or sequence (claims 17-41 and 43-48), or to any cruciferin gene promoter of any sequence (claim 42). No

guidance is presented for any seed-specific regulatory region other than the promoters from three particular structural genes isolated from the same plant family.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the invention as broadly claimed.

See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene (or promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence), and at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

See *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Applicants respectfully traverse the rejection of Claims 17-48 under 35 U.S.C. 112, first paragraph, because in the claimed methods, it is seed specific expression that is essential; a particular promoter or transcription initiation region that is preferentially regulated in plant seed tissue is not essential. In order to satisfy the written description requirement, applicants must convey with reasonably clarity to those skilled in the art that, as of their effective filing date they were in possession of the claimed invention. MPEP 2163.02.

Applicants respectfully refer the Examiner to Example 18 on pages 65-66 of the "Revised Interim Written Description Guidelines Training Materials". Analogous to Example 18, a review of the specification reveals that preferential transcription in a plant seed tissue is essential to the function/operation of the claimed invention. A particular transcriptional initiation region is not essential to the claimed invention: it is important only that the transcriptional initiation region is from a gene that is preferentially transcribed in plant seed tissue. Claim 42 has already been found by the Examiner to be novel and unobvious. As described by applicants below, the remaining claimed methods also are novel and unobvious. The claims are drawn to a genus, i.e. any of a variety of methods that can be used for transcribing a gene of interest preferentially in plant seed tissue. There is actual reduction to practice of four embodiments, including preferential expression in seed tissue of a DNA sequence of

interest by subcloning into a DNA construct having (i) a napin promoter from *Brassica napus*, (ii) a napin promoter from *Brassica campestris*, (iii) an acyl carrier protein (ACP) promoter from *Brassica campestris*, and (iv) an EA9 promoter from *Brassica campestris*. The art indicates that there is no substantial variation within the claimed genus because there are a limited number of ways to practice the process steps of the invention. The four working embodiments are representative of the genus based upon the disclosure of a napin, an ACP or an EA9 promoter as a system for preferential seed tissue transcription, considered along with the level of skill and knowledge in the art. Applicants respectfully submit that the skilled artisan would recognize Applicants' possession of all the various expression methods necessary to practice the claimed invention, therefore the claimed invention is adequately described.

The Examiner has cited *Amgen Inc. v. Chugai Pharmaceutical co. Ltd.*, 18 USPQ 2d 1016 in support of this Written Description rejection. Applicants respectfully submit that this particular case is not relevant to the instant application because the claims in question were all directed to compositions (cDNA sequences for erythropoietin). In the second paragraph of column 1 on page 1020, it is stated that "the 4,703,008 patent does not contain a process claim, an issue that is not now before us." The statement cited by the Examiner on page 1021 is in the context of a 102 rejection and addresses claims to a "purified and isolated DNA sequence". The statement recited by the Examiner on page 1027 is in the context of a 112 *enablement* rejection of a broad generic composition claim directed to DNA sequence analogs. Nowhere does this case address a method claim of any kind or a written description rejection. Applicants respectfully assert that this case is not applicable for properly evaluating the claims of the instant application.

Further, in *University of California v. Eli Lilly and Co.*, also cited by the Examiner, the issues addressed by the court relate only to composition claims, not to process claims. Also, in the patent in suit in *UC v. Eli Lilly*, working examples were not provided (*see* col. 1, lines 1-4 on page 1405), whereas, in contrast, the instant

application provides numerous successful working examples. Applicants respectfully assert that possession of the claimed invention has been demonstrated as both conception and reduction to practice have occurred. Because the specification demonstrates possession of the claimed methods, Applicants respectfully request the Examiner to withdraw this rejection.

35 U.S.C. § 102(b)

Claims 28-29, 31 and 46-47 are rejected under 35 U.S.C. § 102(b) as being anticipated by each of Horsch et al. and DeBlock et al. Each of Horsch et al. and DeBlock et al. teach plants and their progeny which contain an *Agrobacterium*-introduced DNA construct comprising T-DNA and a constitutive opine synthase promoter expressible in any tissue including seeds and a heterologous gene encoding an enzyme conferring antibiotic resistance, wherein the production of seeds would be an inherent feature of the production of progeny, and wherein said promoters are "regulatable" by being capable of being activated. Note that page 11 of the instant specification, lines 11-29 characterize the opine synthase promoters as being encompassed by the invention.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference. MPEP 2131. These rejections are respectfully traversed because the nopaline synthase promoter disclosed by Horsch and DeBlock directs equivalent gene transcription throughout several different plant tissues including leaves, shoots, roots, seeds, and stems, but is neither regulated in a plant seed tissue (the claims prior to amendment) nor does it show a demonstrated preference for any one tissue (*see* for example DeBlock, *et al.*, Figure 5, p. 1685) (the claims as amended). Because Horsch and DeBlock are each limited to a disclosure of a promoter that equivalently expresses in several plant tissues but preferentially in none, neither of these references teaches each and every aspect of the claimed inventions as set forth in Claims 28-29, 31 and 46-47. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

35 U.S.C. § 103(a)

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the

contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Applicants confirm that the subject matter of the various claims was commonly owned at the time any inventions covered herein were made.

Claims 17-32, 34-37, 39-40, and 43-48 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zambryski et al. taken with Sengupta-Gopalan et al.

Zambryski et al. teach a method of tumor-free transformation comprising plant infection with tumor gene-free Agrobacterium strains containing genes for opine synthase and antibiotic resistance under the control of a plant-expressible promoter, and suggest the wise use of this method for the introduction of heterologous genes into plants (see, e.g., paragraph bridging pages 2143 and 2144; page 2145, column 1, second full paragraph; paragraph bridging pages 2148 and 2149; page 2149, column 1).

Zambryski et al do not teach the use of seed-specific promoters.

Sengupta-Gopalan et al. teach the function of the seed-specific phaseolin promoter in seeds of a heterologous plant, identify the exact correspondence of phaseolin cDNA and phaseolin mRNA in transformed tobacco cells (from which the transcription start site of the native phaseolin gene could have been deduced, thereby enabling deduction of the upstream promoter region), and suggest the use of the technique for the obtention of tissue-specific expression of a variety of heterologous genes in a variety of crop plants (see, e.g., page 3321, column 1; page 3322, column 1, top paragraph; page 3324, column 2, top paragraph).

It would have been obvious to one of ordinary skill in the art to utilize the method of plant transformation taught by Zambryski et al. and to modify that method by incorporating the phaseolin promoter taught by Sengupta-Gopalan . and to modify that method by incorporating the phaseolin promoter taught by Sengupta-Gopalan et al., as suggested by Zambryski et al. and Sengupta-Gopalan et al. Choice of transformable and regenerable plant species or gene of interest would have been the optimization of process parameters. Thus, the claimed invention was clearly *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Applicants respectfully traverse the rejection of Claims 17-32, 34-37, 39-40 and 43-48 as *prima facie* obvious over Zambryski in view of Sengupta-Gopalan under 35 U.S.C. 103(a), because individually or combined, these two references do not teach or suggest all of the limitations of the claimed invention. MPEP 2142. Independent Claims 17, 18, 28, 34, 39, 46 and 48 all recite two required elements of the DNA construct that is genomically integrated into a plant host cell as part of the claimed methods. Neither Zambryski nor Sengupta-Gopalan either individually or combined teach or suggest genomically integrating into a host cell a DNA construct having as

operably linked components (1) a promoter or transcriptional initiation region from a gene that is preferentially or specifically expressed in plant seed tissue and (2) a DNA sequence of interest *other than the coding sequence native to the promoter or transcriptional initiation region of element 1.*

Zambryski discloses transforming tobacco plants with the pGV3850 plasmid that has a sequence encoding nopaline synthase under the control of its native and tissue non-specific nopaline synthase promoter and a sequence encoding for β-lactamase (ampicillin resistance) under the control of a bacterial promoter that is non-functional in plants. Zambryski proposes using the pGV3850 plasmid containing sequences from the bacterial plasmid pBR322 as a general recipient for any foreign gene of interest (Figure 5 on page 2148). In the last paragraph of column 2 on page 2148, Zambryski discloses that Herrera-Estrella cloned four different coding sequences behind the tissue-non-specific nopaline synthase promoter. In the final paragraph on page 2149, Zambryski proposes, as an invitation for further investigation, asking questions about tissue-specific regulation of genes, and suggests monitoring the effects of transferring completely foreign genes (where a gene includes a promoter and its native coding sequence) into plants, or studying genes isolated from particular cell types. Nowhere does Zambryski teach or suggest transforming plants with a construct having as operably linked components a transcriptional initiation region from a gene that is preferentially expressed in plant seed tissue and a DNA sequence of interest other than the coding sequence native to that transcriptional initiation region.

Adding Sengupta-Gopalan does not cure the deficiencies of Zambryski. Sengupta-Gopalan discloses expressing the bean β-phaseolin gene under the control of its native phaseolin promoter in tobacco plants. Sengupta-Gopalan demonstrate that bean β-phaseolin regulated under the control of its native promoter is expressed preferentially in the seeds of tobacco plants. In the first paragraph in column 2 on page 3324, Sengupta-Gopalan state that their results "confirm the value of Ti plasmids as gene vectors for higher plants and fully support the practical potentials that have been

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envisaged for foreign gene expression in agriculturally important plants". Sengupta-Gopalan proposes expressing foreign genes (which include a promoter and its native coding sequence) in plants, and cites Murai for expressing the β-phaseolin gene under the control of the tissue non-specific octopine synthase promoter (page 3320, column 1), but nowhere is it suggested or implied to express a non-β-phaseolin coding sequence under the control of the β-phaseolin promoter. In fact, Sengupta-Gopalan does not even define the promoter region in the β-phaseolin gene sequence used to transform tobacco plants. Nowhere does Sengupta-Gopalan teach or suggest transforming plants with a construct having as operably linked components a transcriptional initiation region from a gene that is preferentially expressed in plant seed tissue and a DNA sequence of interest other than the coding sequence native to that transcriptional initiation region.

In summary, it is submitted that neither Zambryski nor Sengupta-Gopalan, either alone or in combination, teach or suggest all the required elements of Claims 17-32, 34-37, 39-40 and 43-48, and that a *prima facie* obviousness rejection under 103(a) in view of these references can not be considered proper. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Claims 20, 33, 38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zambryski et al. taken with Sengupta-Gopalan et al. as applied to claims 17-32, 34-37, 39-40 and 43-48 above, and further in view of Pedersen et al.

Zambryski et al. taken with Sengupta-Gopalan et al. teach the method of tumor gene deletion and gall-free Agrobacterium-mediated transformation for the expression of heterologous genes under the control of seed-specific promoters as discussed above, but do not teach soybean transformation.

Pedersen et al. teach the injection of soybean plants with Agrobacterium to effect transformation (see, e.g., page 201, column 2, third full paragraph; page 203, column 1, bottom paragraph, Figure 4).

It would have been obvious to one of ordinary skill in the art to utilize the method of tumor gene deletion and gall-free Agrobacterium-mediated transformation for the expression of heterologous genes under the control of seed-specific promoters taught by Zambryski et al taken with Sengupta-Gopalan . taken with Sengupta-Gopalan et al, and to modify that method by incorporating the soybean-infecting Agrobacterium plasmid taught by Pedersen et al. given the recognition by those of ordinary skill in the art that each would have continued to function in its known and expected manner, and the recognition of the benefits of transforming a wide variety of plant species including soybean as suggested by Sengupta-Gopalan et al. Thus, the claimed invention was clearly *prima facie*

obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Applicants respectfully traverse the rejection of Claims 20, 33, 38 and 41 as *prima facie* obvious over Zambryski in view of Sengupta-Gopalan and Pedersen, because whether taken individually or combined, these references do not teach or suggest all the required elements of the claimed methods. Claim 20 depends from Claim 17 or 18; Claim 33 depends from Claim 28; Claim 38 depends from Claim 34; Claim 41 depends from Claim 39. Claims 20, 33, 38 and 41 all recite two required elements of the DNA construct that is genomically integrated into a plant host cell as part of the claimed methods. Not one of Zambryski, Sengupta-Gopalan or Pederson either individually or combined teach or suggest genomically integrating into a host cell a DNA construct having as operably linked components (1) a promoter or transcriptional initiation region from a gene that is preferentially or specifically expressed in plant seed tissue and (2) a DNA sequence of interest *other than the coding sequence native to the promoter or transcriptional initiation region of component 1.*

As stated above, neither Zambryski nor Sengupta-Gopalan disclose or suggest transforming a plant with a construct having as operably linked components a promoter preferentially regulated in a plant seed tissue and a DNA sequence of interest other than the coding sequence native to that promoter. Combining Zambryski and Sengupta-Gopalan with Pedersen does not cure their deficiencies. Pedersen discloses transforming soybean plants with plasmids containing T-DNA fragments from a nopaline-producing *Agrobacterium tumefaciens* strain. These plasmids express nopaline synthase under the control of the native, non-tissue specific nopaline synthase promoter. Pedersen does not teach anything about using open reading frames and promoter regions as separable components. Like Zambryski and Sengupta-Gopalan, Pedersen does not teach or suggest transforming a soybean plant with a construct having a transcriptional initiation region preferentially expressed in plant seed tissue and a DNA sequence of interest other than the coding sequence native to that

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transcriptional initiation region. Because the individual or combined references of Zambryski, Sengupta-Gopalan and Pedersen do not teach or suggest all the required elements of Claims 20, 33, 38 and 41, a *prima facie* obviousness rejection in view of these references can not be considered proper. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

> **Claims 17-32, 34-37, 39-40 and 43-48 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hall et al. (U.S. Patent 5,504,200) taken with Sengupta-Gopalan et al.**
>
> **Hall et al. teach the Agrobacterium-mediated transformation of sunflower, alfalfa and tobacco cells with a heterologous phaseolin promoter and phaseolin structural gene, wherein expression of the phaseolin gene is highly regulated and seed-specific in the native bean, wherein intronless phaseolin genes were also constructed, wherein deletions of the tumor genes on the Ti plasmid were performed, and wherein whole tobacco plants were recovered which expressed high levels of the protein in the seed in the same pattern in which it was expressed in the native bean (see, e.g., column 9, lines 55-68; column 10, lines 1-16 and 57-59; column 19, lines 3—67; columns 2—21; column 22, lines 1-41; column 24, lines 9-61; columns 28-31, especially column 29, lines 1-5 and 60-68). Hall et al also teach phaseolin cDNA from which the transcription initiation region of the native gene, and the upstream promoter, could have been deduced if desired (see, e.g., column 19, lines 57-67; column 20, lines 1-7). Hall et al. also teach the transformation of alfalfa cells with a chimeric gene comprising the nopaline synthase promoter and a gene encoding the neomycin phosphotransferase enzyme, and suggest the transformation of a variety of plants with a plant gene-derived promoter such as the phaseolin promoter and a variety of structural genes, such as genes conferring disease resistance, herbicide resistance, or flavor components (see, e.g., column 24, lines 9-61; column 10, lines 45-59; and claims 11-30).**
>
> **Hall et al. do not explicitly teach a chimeric gene construct comprising the phaseolin promoter and a heterologous structural gene.**
>
> **Sengupta-Gopalan et al. teach that a heterologous gene comprising the phaseolin promoter and phaseolin structural gene is expressed in a highly seed-specific manner in the heterologous species tobacco following Agrobacterium-mediated transformation, and that the phaseolin promoter contains all of the necessary components for seed-specific expression; and suggest the value of tissue-specific heterologous gene expression in transformed plants (see, e.g., page 3320, Abstract; page 3321, Table 1 and column 1; page 3323, column 2, third full paragraph; page 3324, column 2, top paragraph).**
>
> **It would have been obvious to one of ordinary skill in the art to utilize the phaseolin promoter which functions in a variety of heterologous plant species as taught by Hall et al for the seed-specific expression of a variety of heterologous genes such as the neomycin phosphotransferase gene taught by Hall et al. in a variety of heterologous plants, as suggested by Hall et al. and Sengupta-Gopalan et al. Choice of heterologous plant species or heterologous structural gene would have been the optimization of process parameters. Thus, the claimed invention was clearly *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.**

Applicants respectfully traverse the rejection of Claims 17-32, 34-37, 39-40 and 43-48 as *prima facie* obvious over Hall in view of Sengupta-Gopalan, because whether taken individually or combined, these references do not teach or suggest transforming a

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plant with a DNA construct that has the required elements of a transcriptional initiation region from a gene that is preferentially expressed in plant seed tissue and a DNA sequence of interest other than the coding sequence native to that transcriptional initiation region. Hall discloses transforming sunflower, alfalfa and tobacco plants with a plasmid encoding the bean β-phaseolin promoter operably linked to its native β-phaseolin coding sequence (with and without introns). Not only does Hall not teach a chimeric gene construct comprising the phaseolin promoter and a heterologous structural gene, as the Examiner states, but Hall's disclosure is inconsistent with potentially using the β-phaseolin promoter for methods requiring seed-specific expression. Although in Column 10, lines 7-8 Hall states that phaseolin is made essentially only while seed is developing within the pod, Hall discloses that transfer of the functional phaseolin gene to alfalfa plants introduces storage protein synthesis *into leaf material* (Column 14, lines 11-14). Based on what Hall teaches, the bean phaseolin promoter is not seed specific. Furthermore, in Column 29, lines 63-66, Hall teaches that "the fact that phaseolin was similarly degraded in germinating tobacco seed showed that *the phaseolin gene product* was tissue specific both with respect to location and function" (emphasis added). This statement conflicts with what Applicants consider to be an essential attribute of the claimed methods: that seed-specific expression is achieved through using the promoter region from a gene that is preferentially expressed in plant seed tissue. In Column 10, lines 45-59, Hall discloses demonstrating expression of a gene from a promoter exogenous to T-DNA within a T-DNA sequence and suggests other useful exogenous plant genes (that include a promoter and a native coding sequence) that could be expressed from within a T-DNA sequence that is introduced into plants. However, Hall does not teach or suggest expressing these useful plant genes under the control of a non-native promoter from a gene that is preferentially expressed in plant seed tissue.

Sengupta-Gopalan does not cure the deficiencies of Hall. Sengupta-Gopalan disclose seed specific regulation of bean β-phaseolin expressed in tobacco plants under

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the control of its native β-phaseolin promoter. Although Sengupta-Gopalan cite Murai for expressing β-phaseolin under the control of the tissue non-specific octopine synthase promoter, Sengupta-Gopalan assess their own results as supporting "the practical potentials that have been envisaged for foreign gene expression in agriculturally important plants." A foreign gene includes both a promoter region and a native coding sequence. Nowhere does Sengupta-Gopalan teach or suggest transforming a plant with a DNA construct having as operably linked components a transcriptional initiation region from a gene that is preferentially expressed in plant seed tissue and a DNA sequence of interest other than the coding sequence native to that transcriptional initiation region. Because the individual or combined references of Hall and Sengupta-Gopalan do not teach or suggest each required element of the methods of Claims 17-32, 34-37, 39-40 and 43-48, a *prima facie* obviousness rejection can not be considered proper. Accordingly Applicants respectfully request the Examiner to withdraw this rejection.

Claims 20, 33, 38 and 41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hall et al. (U.S. Patent 5,504,200) taken with Sengupta-Gopalan et al. as applied to claims 17-32, 34-37, 39-40 and 43-48 above, and further in view of Zambryski et al. taken with Pedersen et al.

Hall et al. taken with Sengupta-Gopalan et al. teach the transformation of a variety of plant species including alfalfa with a tumor gene-deleted Agrobacterium tumefaciens vector comprising the phaseolin promoter and heterologous structural gene for seed-specific gene expression as discussed supra, but do not teach soybean transformation.

Zambryski et al. teach a method of tumor-free transformation comprising plant infection with tumor gene-free Agrobacterium strains containing genes for opine synthase and antibiotic resistance under the control of a plant-expressible promoter, and suggest the wide use of this method for the introduction of heterologous genes into plants (see, e.g., paragraph bridging pages 2143 and 2144; page 2145, column 1, second full paragraph; paragraph bridging pages 2148 and 2149; page 2149, column 1).

Pedersen et al. teach the injection of soybean plants with Agrobacterium to effect transformation (see, e.g., page 201, column 2, third full paragraph; page 203, column 1, bottom paragraph, Figure 4).

It would have been obvious to one of ordinary skill in the art to utilize the method of tumor gene deletion and gall-free Agrobacterium-mediated transformation for the seed-specific expression of heterologous structural genes under the control of the phaseolin promoter in a variety of plant species including alfalfa as taught by Hall et al. taken with Sengupta-Gopalan et al., and to modify that method by incorporating the tumor deletion and whole plant regeneration taught by Zambryski et al and the soybean-infecting Agrobacterium plasmid taught by Pedersen et al., given the recognition by those of ordinary skill in the art that each would have continued to function in its known and expected manner, and the recognition of the benefits of transforming a wide variety of plant species including

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soybean, as suggested by Hall et al. taken with Sengupta-Gopalan et al. Thus, the claimed invention was clearly *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Applicants respectfully traverse the rejection of Claims 20, 33, 38 and 41 as *prima facie* obvious over Hall in view of Sengupta-Gopalan and further in view of Zambryski and Pedersen, because whether taken individually or combined, these references do not teach or suggest all the required elements of the claim methods. Claim 20 depends from Claim 17 or 18; Claim 33 depends from Claim 28; Claim 38 depends from Claim 34; Claim 41 depends from Claim 39. Claims 20, 33, 38 and 41 all recite two required elements of the DNA construct that is genomically integrated into a plant host cell as part of the claimed methods. Not one of Hall, Sengupta-Gopalan, Zambryski or Pederson either individually or combined teach genomically integrating into a host cell a DNA construct having as operably linked components (1) a promoter or transcriptional initiation region from a gene that is preferentially or specifically expressed in plant seed tissue and (2) a DNA sequence of interest *other than the coding sequence native to the promoter or transcriptional initiation region of component 1*.

As stated above, neither Hall nor Sengupta-Gopalan disclose anything about transforming a plant with a construct having as operably linked components a promoter preferentially regulated in a plant seed tissue and a DNA sequence of interest other than the coding sequence native to that promoter. Combining Hall and Sengupta-Gopalan with Zambryski and Pedersen does not cure their deficiencies. Zambryski discloses expressing antibiotic resistance genes under the control of a tissue non-specific nopaline synthase promoter. Pedersen discloses transforming soybean plants with plasmids containing T-DNA fragments from a nopaline-producing *Agrobacterium tumefaciens* strain. These plasmids express nopaline synthase under the control of the native, non-tissue specific nopaline synthase promoter. Pedersen does not teach anything about using open reading frames and promoter regions as separable

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components. Not one of Hall, Sengupta-Gopalan, Zambryski or Pedersen teach or suggest transforming a soybean plant with a construct having a transcriptional initiation region preferentially expressed in plant seed tissue and a DNA sequence of interest other than the coding sequence native to that transcriptional initiation region. Because the individual or combined references of Hall, Sengupta-Gopalan, Zambryski and Pedersen do not teach or suggest all the required elements of Claims 20, 33, 38 and 41, a *prima facie* obviousness rejection in view of these references can not be considered proper. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

CONCLUSION

In view of the above amendment and remarks, it is submitted that this application is now ready for allowance. Early notice to that effect is solicited. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 328-4400.

Respectfully submitted,

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